Moreover, clustering of the samples based on the most variable genes showed perfect segregation of samples belonging to the same individual. Clonality and diversity of the T cell repertoire, as well as the proportion of clusters based on the sequence of the T cell receptor sequence, were also highly preserved.
Conclusions: Our data demonstrates a highly preserved PBMC profile at the transcriptome level over cryopreservation time, confirming that biobanked PBMCs are suitable for projects using scRNA-seq on large cohorts.

Disclosure
The authors have nothing to disclose.

EP0941

Immune response against SARS-CoV-2 vaccines in treatment-naive multiple sclerosis patients

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Introduciton: Multiple Sclerosis (MS) is an autoimmune disease with B-cell dysregulation playing an essential role in pathogenesis. As B-cells are also responsible for antibody production, their disfunction could also affect the humoral immune response against SARS-CoV-2 vaccines.
Aims: To compare the immune response after messenger RNA (mRNA) BNT162b2 (Pfizer/BioNTech) and inactivated Coronavac vaccines in newly diagnosed treatment-naive MS (tnMS) patients and healthy controls (HC).
Methods: A single-center cross-sectional study evaluating antibody response against SARS-CoV-2 vaccines (inactivated vs mRNA) in HC and newly diagnosed and treatment-naive MS patients. Serum samples were collected at least two weeks after the second dose of the vaccine. The cutoff level of seropositivity is $\geqslant$ 50 antibody unit (AU)/ml.
Results: 46 participants had two doses of inactivated Coronavac (35 HC and 11 tnMS), and 103 (57 HC and 46 tnMS) had two doses of mRNA. There was no significant difference in antibody response between HC and tnMS in the inactivated vaccine group. In the mRNA group, the antibody titers were significantly higher in HC (p=0.009), though no difference in the seropositivity rates was observed.
Conclusions: Although MS is an autoimmune inflammatory disease, it does not affect immunity against the SARS-CoV-2 vaccine in treatment-naive patients.

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Covid-19 vaccination can induce multiple sclerosis via cross-reactive CD4+ T cells recognizing SARS-CoV-2 spike protein and myelin peptides

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Introduction: Infection with the SARS-CoV-2 coronavirus can lead to a wide range of acute and also chronic disease manifestations. The rapidly developed vaccinations are highly effective in preventing severe disease courses and have been proven safe. Both natural infection and, to a much lower extent, the mRNA-based vaccinations can be accompanied by transient autoimmune phenomena or onset of autoimmune diseases.
Objectives: We report here two cases of multiple sclerosis (MS) with clinical and new radiological signs beginning in close temporal relation to spike (S) protein mRNA-based vaccinations.
Aims: To establish that the onset of MS in these two cases is very likely caused by CD4+ T cell clones that cross-recognize SARS-CoV-2 S protein-derived peptides and peptides derived from myelin proteins, which have previously been implicated in MS.
Methods: Spike specific CD4+ T cells from peripheral blood and CD4+ T cells from CSF sample were isolated and expanded for autoantigen screening test. A list of well-known MS-related autoantigens including immunodominant peptides and isoforms from MBP, MOG, PLP, RASGRP2, TSTA3 peptides were included to assess T cell reactivity. CD4+ CFSElow fraction were sorted after stimulate with positive autoantigen pools or SARS-Cov-2 Spike protein, followed by expansion and testing with autoantigen peptides and Spike protein. Supernatant from cell culture were further analyzed for IFN-gamma secretion.
Results: Self-reactive T cells were detected from Spike specific T cell population in both patients. CD4+ T from CSF also showed reactivity to MBP, MOG, PLP peptide pools. Finally, we found proinflammatory T cell clones that recognize both Spike protein and immunodominant MBP peptides and MOG peptides, which have previously been implicated in MS.
Conclusions: Detailed studies of both peripheral blood- and CSF-derived CD4+ T cells show that the onset of MS in these two cases is very likely caused by CD4+ T cell clones that cross-recognize SARS-CoV-2 S protein-derived peptides and peptides derived from myelin proteins, which have previously been implicated in MS.

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Neuway, CellProtect, Third Rock; patent holder and co-holder on patents of: daclizumab in MS, JCV VP1 for vaccination against PML; JCV-specific neutralizing antibodies to treat PML; antigen-specific tolerization with peptide-coupled cells and novel autoantigens in MS; co-founder of Abata, co-founder and co-owner of Cellerys®

Pathology and pathogenesis of MS - Microbiology and virology

EP0943

Serum antiviral antibody titers in multiple sclerosis patients after six months under teriflunomide treatment and their clinical implications: a longitudinal study

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Introduction: Epstein-Barr virus (EBV) and Human herpesvirus 6 (HHV-6) have been associated with multiple sclerosis (MS). Teriflunomide is an oral disease modifying therapy approved for treatment of relapsing forms of MS. In the preclinical Theiler's Murine Encephalitis Virus model of MS, the drug demonstrated an increased rate of viral clearance versus the vehicle placebo. Furthermore, teriflunomide inhibits lytic EBV infection in vitro.

Objectives: 1. To evaluate the variation of IgG antibody titers against EBNA-1 and VCA of EBV and IgG and IgM against HHV-6 in serum between baseline visit (no treatment) and after 6 months of teriflunomide treatment, as part of their regular clinical follow-up. 2. To correlate this variation with the clinical response (relapses and progression) and radiological response (variation in the lesion load in T2 and number of Gadolinium-enhancing lesions) after 12 months and 24 months of treatment with teriflunomide.

Methods: A total of 101 MS patients (62 females; mean age: 43.4 years) with one serum sample at baseline visit (prior teriflunomide onset) and another serum sample after 6 months of teriflunomide treatment were recruited: 80 had been treated at least 24 months, 13 had stopped teriflunomide before 24 months and 8 were currently under teriflunomide therapy but with less than 24 months of follow-up. We analyzed the levels of the viral antibodies titers above mentioned in serum samples with ELISA commercial kits, following manufacturer instructions.

Results: 1. After 6 months of teriflunomide treatment antiviral antibodies titers decreased in: 60/100 (60%) MS patients for HHV-6 IgG, 74/100 (74%) for HHV-6 IgM, 74/101 (73.3%) for EBNA-1 IgG and 69/100 (69%) for VCA IgG. 2. Among the 80 MS patients that fulfilled 24 months under teriflunomide therapy: 13/21 (61.9%) of MS patients with EBNA-1 IgG titers increased after 6 months treatment experienced EDSS increase and/or relapses vs. 22/59 (37.3%) of MS patients without EBNA-1 IgG increased ($p=0.05$; O.R.=2.7). No associations were found for HHV-6 or VCA of EBV.

Conclusions: Teriflunomide significantly reduced the levels of IgG antibody titers against EBNA-1 and VCA of EBV and IgG and IgM against HHV-6 after 6 months of treatment in a real-life cohort of Spanish MS patients. Increased in EBNA-1 IgG titers after 6 months of treatment was associated with a higher probability of experiencing EDSS increase and/or relapses after 2-years under teriflunomide therapy.

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